REMARKS

Applicants have canceled claims 1-15 simply for purposes of pursuing them by way of a continuation application, and in so doing, expediting prosecution of claims 16-38. Claim 16 has been amended to further define the hydrocortisone or derivative thereof as being present (in the composition) in the amount of "about 0.01 percent to about 5 percent" by weight of the composition, support for which is set forth on page 4 (para. 12) of the specification." Claims 19, 20 and 21 have been amended simply to show antecedent basis for the recitation "amount". Claims 35-38 have been amended to further define the steroidal hormone or anti-inflammatory agent as "hydrocortisone or a derivative thereof," and which is present in the composition an amount of "about 0.01 to about 5 % by weight of the composition." No new matter has been added. Accordingly, entry of the amendment is requested.

Claims 1-3, 5, 6, 8, 10, 11, 16, 22, 23, 25, 27, 28, and 29 have been rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 6,113,888 to Castro, *et al.* ("*Castro*").

Not withstanding the fact that *Castro* does not anticipate any of the rejected claims, Applicants submit that the rejection is moot as it applies to claims 1-3, 5, 6, 8, 10, and 11. Applicants also submit that the teachings of *Castro* do not anticipate claims 16, 22, 23, 25, 27, 28, and 29, in their original or amended form.

Castro teaches self-tanning mousse compositions that may contain, as optional ingredients, *inter alia*, a humectant such as glycerin, 1,2-pentanediol, and 2-methyl-1,3-propane diol. See, *e.g.*, Column 2, lines 43-45, and Column 5, lines 48-56 in *Castro*. Additional optional ingredients, disclosed on Columns 4-5, include a variety of "dermatologically active agents," including agents for treating wound healing,

inflammation, acne, psoriasis, cutaneous aging, skin cancer, impetigo, herpes, chickenpox, dermatitis, pain, itching, and skin irritation. Hydrocortisone is disclosed on Column 4, line 65, as one of many such agents. On the other hand, there is no disclosure in *Castro* of a specific self-tanning mousse composition that contains pentylene glycol and hydrocortisone or a derivative thereof. Thus, in order to arrive at the claimed invention, the person of ordinary skill in the art would have to pick and choose from among two different types of optional ingredients. According to the Court of Appeals for the Federal Circuit, such disclosures do not constitute an anticipation so as to negate novelty under 35 U.S.C. § 102. *See, Akzo N.V. v. U.S. Intern. Trade Com'n*, 808 F.2d 1471, 1481, 1 USPQ2d 1241, 1245-46, (Fed. Cir. 1986)("The ALJ also rejected appellants' arguments that the Blades process was anticipated by the Hill and Smith patents which were referenced in the Morgan '645 patent. This would have required Blades to randomly pick and choose among a number of different polyamides, a plurality of solvents, and a range of inherent viscosities. The ALJ rejected such 'random picking and choosing' of prior art, relying on *In re Arkley*, 455 F.2d 586, 587, 172 USPQ 524, 526 (CCPA 1972), and concluded in effect that the anticipatory reference must disclose in the prior art a thing substantially identical with the claimed invention.")

In view of the foregoing, Applicants submit that *Castro* does not anticipate claims 16, 22, 23, 25, 27, 28, or 29, even in their original unamended form. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Claims 4, 7, 9, 12-15, 17-21, 24, 26, and 30-38 have been rejected under §103(a) as being unpatentable over *Castro* as applied to claims 1-3, 5, 6, 8, 10, 11, 16, 22, 23, 25, 27, 28, and 29 above, in view of U.S. Patent 4,552,872 to Cooper, *et al.*

("*Cooper*"), U.S. Patent 6,075,056 to Quigley, *et al.* ("*Quigley*"), and further in view of U.S. Patent 6,274,124 to Vollhardt ("*Vollhardt*"). *Castro* is alleged not to teach hydrocortisone acetate, triamcinolone acetate, and their respective percentages in the compositions, or butylene glycol or a mixture of butylene glycol and propylene glycol as additional solvents. *Cooper* is alleged to supply these teachings. *Quigley* is alleged to teach topical formulations that may be in the form of creams, ointments, gels, lotions, foams, powders, shampoos, and/or liquid solutions comprising a steroid (0.01-2.5 percent by weight) and a propylene glycol (5-20 percent by weight), wherein the steroid can be triamcinolone acetate. *Vollhardt* is alleged to teach cosmetic and/or dermatological formulations comprising 1,2-pentanediol and at least one cosmetic or dermatological active agent in a cosmetically and/or pharmaceutically acceptable carrier for topical application to the skin, wherein the 1,2-pentanediol should preferably be present in an amount of 0.5 percent to 6 percent by weight of the composition gives improved water resistance to the compositions as compared to 1,2-propanediol and 1,2-hexanediol, and wherein the cosmetics and/or dermatologically active agents include steroidal anti-inflammatory agents such as hydrocortisone, non-steroidal anti-inflammatory agents, anti-microbrial agents in fragrances.

The Examiner has determined that it would have been obvious that 1,2-pentanediol could be used in the topical pharmaceutical corticosteroid compositions of *Cooper*, in view of *Vollhardt*, as *Castro* demonstrated that 1,2-pentanediol could be combined with another diol (propylene glycol or butylene glycol or both), and that *Castro*, *Cooper*, *Cooper*, and *Vollhardt's* compositions all contain the same dermatologically active agents (steroidal anti-inflammatories). The increased water resistance properties of 1,2-pentanediol-containing compositions would have

motivated one of ordinary skill in the art to combine the compositions. A reasonable chance of success would have been expected as the compositions demonstrated that 1,2-pentanediol can be combined with additional diols in all the compositions detailed include steroidal anti-inflammatory agents exemplified by hydrocortisone. Applicants respectfully disagree with the determination that the claimed invention would have been obvious.

Applicants submit that the rejection is moot with respect to claims 4, 7, 9 and 12-15. Applicants also submit that claims 17-21, 24, 26 and 30-38 would not have been obvious to a person skilled in the art. As described in the specification, Applicants' claimed invention achieves unexpected results, particularly in terms of enhanced penetration of hydrocortisone through the skin and resulting bioavailability.

Turning to the cited publications, *Cooper* is directed to topical compositions containing a corticosteroid and a penetration-enhancing vehicle containing as one element, a C3-C4 diol. On col. 2, lns. 43-45, *Cooper* teaches that the size and shape of corticosteroids makes them exceedingly difficult to deliver percutaneously. Cooper and his co-inventors discovered that a select number of combinations of a binary penetration system containing a cell-envelope disordering compound and a C3-C4 diol, previously thought to be useful only in delivering non-steroidal varieties of anti-inflammatory actives and select substituted adenosine- and guanine-derived anti-virals, could consistently and dramatically improve topical delivery of certain corticosteroids (*Cooper*, col., 3, lns. 1-12). Hydrocortisone and various derivatives are included among the agents whose penetration could be enhanced by such combinations. See, cols. 7-8. *Cooper* does not teach the C5 diol, pentylene glycol. In addition, none of the summaries of the prior art provided on cols. 3-4 of *Cooper* contains any mention of the C5

diol. Plainly, *Cooper* provides absolutely no motivation to use pentylene glycol in combination with hydrocortisone for topical application, and if anything, teaches away from a C5 diol.

Quigly is directed to stable topical formulations containing an antifungal agent and an anti-inflammatory steroid. There is no disclosure of hydrocortisone or its derivatives. Among the excipients (*e.g.*, solvents, emollients, humectants and emulsifiers) disclosed on cols. 2-3 and elsewhere, there is no mention of pentylene glycol.

Vollhardt is directed to imparting or improving water resistance to a cosmetic/dermatological composition by adding 1,2-pentane diol (which in Table 1, is disclosed as synonymous with "pentylene glycol"). The compositions are typically sunscreens, but as disclosed on cols. 4-5 they are not limited to sunscreens and may contain an active agent, *e.g.*, antioxidant, anti-inflammatory compound (*e.g.*, hydrocortisone on col. 4, ln. 67), anti-microbial compound, antiperspirant, fragrance, or skin whitening compound. There is no disclosure of the recited range of amounts of hydrocortisone, or any specific example of a composition containing pentylene glycol and hydrocortisone, let alone in an amount that falls within the claimed range.

Thus, none of the cited prior art publications teaches a composition comprising hydrocortisone or a derivative thereof, and pentylene glycol, wherein the hydrocortisone is present in an amount of from 0.01 percent to about 5 percent by weight of the composition, or methods of making the composition or using it. Applicants submit the collective prior art teaches away from the claimed invention.

The determination of whether a claimed invention would have been obvious or not requires an analysis of 4 factual inquiries which, as set forth on page 4 of the Office action, include a consideration of objective evidence present in the

application. As described in the present patent application, the claimed invention achieves several unexpected results. These results flow from Applicants' discovery that hydrocortisone and its derivatives are more soluble in pentylene glycol than other polyols such as glycerol, propylene glycol, butylene glycol and hexylene glycol. More specifically, as shown in Example 1 on page 11, Applicants discovered that hydrocortisone is about two times more soluble in pentylene glycol than in hexylene glycol, about 1.5 times more soluble in pentylene glycol than in propylene glycol, and about 1.25 times more soluble in pentylene glycol than in butylene glycol. As taught in the present specification, there are at least three unexpected benefits that flow from the combination of pentylene glycol and hydrocortisone and its derivatives, namely aesthetic appeal, less tackiness and greater bioavailability. The first two advantages are described on pages 5-6 as follows:

> Due to the greater solubility of the active agents pentylene glycol, the amounts of the other solvents are significantly lower, e.g., about 20 to 95 percent less than if pentylene glycol were not present. Relatively high amounts of glycols are undesirable from several standpoints, especially in terms of aesthetic appeal and tackiness. In contrast, compositions of the present invention are more aesthetically acceptable and have less tackiness.

In Example 7 on pages 16-18 of the specification, Applicants compared the rate of release of hydrocortisone from various commercially available one percent hydrocortisone anti-itch creams and ointments. The results show that the release rate of hydrocortisone from a gel of the present invention was about 100 times greater than the commercial products, none of which contains pentylene glycol. As described in paragraph 34 on page 18, and illustrated in Fig. 1, the results also show that the compositions of the present invention provided greater availability of the active agent to penetrate the affected area

on the skin or scalp, and thus provided greater bioavailability of the active agent.

These results would not have been expected based on the collective teachings of the prior art, particularly *Cooper* and *Vollhardt*. By limiting the diols specifically to C3 and C4 diols, *Cooper* clearly teaches away from the claimed invention. *Vollhardt*'s objective was to increase water resistance or in other words, the amount of time that the active agent actually stays on the surface of the skin. Increasing water resistance does not equate with increasing solubility and bioavailability. As explained in the accompanying Declaration of Dr. Hani Fares, a named co-inventor, the present inventors sought to increase solubility of hydrocortisone and the rate and/or extent of penetration through the skin barrier. In so doing, they unexpectedly discovered that hydrocortisone is more soluble in pentylene glycol than in other diols. The claimed invention achieves unexpected results, namely greater aesthetic appeal, less tackiness, and greater penetration and bioavailability of hydrocortisone, compared to other commercial hydrocortisone topical formulations. Increasing water resistance and retention on the skin, which were *Vollhardt*'s objectives, are completely different and even opposite the properties the present inventors were seeking, namely increased solubility, penetrability and bioavailability.

In view of the foregoing, Applicants submit that the claimed invention would not have been obvious over the collective teachings of the cited prior art. Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he/she telephone applicant's attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefore.

Dated: March 29, 2005

Respectfully submitted,

By Shawn P. Foley

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